(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 0 726 791 B1

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:
21.06.2000 Bulletin 2000/25

(21) Application number: **92917047.0**

(22) Date of filing: **31.07.1992**

(51) Int. Cl.^{7}: **A61N 1/18**, A61N 1/08

(86) International application number:
PCT/US92/06207

(87) International publication number:
WO 93/02740 (18.02.1993 Gazette 1993/05)

(54) IMPLANTABLE TISSUE STIMULATOR

IMPLANTIERBARES GEWEBEREIZUNGSGERÄT

STIMULATEUR TISSULAIRE IMPLANTABLE

(84) Designated Contracting States:
DE FR GB IT NL SE

(30) Priority: **31.07.1991 US 738801**

(43) Date of publication of application:
21.08.1996 Bulletin 1996/34

(73) Proprietor: **Cyberonics, Inc.**
Houston, TX 77058 (US)

(72) Inventor: **BAKER, Ross, G., Jr.**
Webster, TX 77025 (US)

(74) Representative:
Haft, von Puttkamer, Berngruber, Czybulka
Patentanwälte
Franziskanerstrasse 38
81669 München (DE)

(56) References cited:
US-A- 3 746 006 **US-A- 4 738 250**

EP 0 726 791 B1

Printed by Xerox (UK) Business Services
2.16.7 (HRS)/3.6

Description

[0001] The present invention relates to a body implantable, battery operated nerve tissue stimulator according to the preamble of claim 1. The invention relates generally to excitable tissue stimulation, and more particularly to improvements in energy efficiency of implantable neurostimulators utilized in conjunction with one or more electrodes which are surgically implanted on a selected nerve or nerves of the patient to permit electrical stimulator thereof.

[0002] Implantable neurostimulators employ one or more batteries as the power source for the device. When the power is depleted, it becomes necessary to perform surgical removal and replacement of the device; It is desirable, therefore, to conserve device energy to the extent possible, while suppling stimulation as needed, in order to prolong device lifetime and increase the interval between surgical replacements. Of course, such considerations are important for any implantable medical device, not merely neurostimulating devices. Ideally, cardiac and neuromuscular stimulators have output circuits which may characterize them as constant current devices. In practice, however, presently available implantable versions of these devices depart significantly from the constant output ideal models.

[0003] The constant current mode of the existing devices has the advantage that changes in system resistance or impedance do not affect the output current of the device. For neurostimulation, this is important because it is the current applied to the nerve which causes excitable fiber depolarization. The constant current mode also tends to limit the possibility of damage to the nerve being stimulated. Nerve damage might occur, for example, from any overstimulation resulting from changes in system impedance that cause current varia-tons.

[0004] Despite its advantages, however, constant current stimulation has certain drawbacks. A constant output current system generally requires that the supply voltage must be significantly greater than the voltage which is actually delivered to the nerve electrode. This excess voltage is dropped across the constant current regulating circuit and may represent significant energy waste, which for reasons noted above, results in the need for undesirably frequent replacements of implanted systems. Another problem is the excess energy consumption in the control circuit of the constant current system. Thsi circuit is required to have a sufficiently rapid response time to permit controlling the output current during even very brief output pulses. Therefore, amplifier bias currents must be set relatively high, with consequent energy overhead. The control circuit may be designed without an active amplifier, but would then possess the disadvantage of requiring even greater supply voltage overhead.

[0005] US-A-4,738,250 describes an external, i.e. not implanted nerve tissue stimulator for stimulation of living tissue which is primarily intended to avoid unidirectional current flow in treating the tissue. During the treatment session, the electrodes used to deliver the treatment signal are positioned and repositioned. The current flow of a controlled voltage wave is kept within desired parameters of current and voltage, and the maximum magnitude of the current flow is limited to a level below that which would damage a typical cell in the path of the flow. Usually the optimal range of the current is limited to 500 to 600 microamperes and a maximum of 900 microamperes. If the maximum level is exceeded or even if the measured parameters differ from the parameters selected by for example plus or minus 15 %, the treatment is aborted by dropping the voltage across the electrodes to zero. Therefor, this patent does not truly disclose or teach a constant current source or any constant output parameter device as desired.

[0006] US-A-3,746,006 discloses a controlled energy output implantable pacer having the constructive features as defined in the preamble of claim 1. Said pacer delivers stimulation pulses to the heart and controls the heart frequency of the patient.

[0007] A problem of pacers results from battery deterioration combined with the fixed pulse width of the heart beat stimulation pulse. The energy of the stimulation pulse will decrease as the battery voltage decreases. According to this patent the width of stimulation pulses is reduced strictly as a function of diminishing battery voltage, to maintain the energy delivered in the stimulation pulses approximately constant.

[0008] It is an object of the present invention to provide an implantable nerve tissue stimulator having reduced energy overhead and producing desired stimulation of the tissue without significant energy losses.

[0009] According to the invention these objects are achieved by the features of claim 1.

[0010] The present invention provides an implantable neurostimulator which encompasses two modes of output circuit operation, each of which combines at least some of the advantages of constant current devices with the greater efficiency of constant voltage devices. Specifically, the output circuit of the neurostimulator pulse generator according to the present invention employs either of two operating modes; namely, (i) a current stabilization mode or (ii) a charge stabilization mode.

[0011] The neurostimulator generates a desired signal, typically a pulse waveform having preprogrammed parameter values, which is delivered via an electrode array implanted on a nerve or nerves of a patient, to excite the cell membranes in the nerve tissue and thereby modulate the electrical activity of the nerve in the desired manner. In the preferred embodiment of a current stabilization mode system, the neurostimulator pulse generator generates a sequence of output pulses or output pulse bursts according to a predetermined pattern, and a control loop connected to the pulse gen-

erator measures the magnitude of the current in the output pulses on a sampled basis, compares the sampled current value to a prescribed target value, and adjusts the voltage of the output pulses to reduce or eliminate any discrepancy between the two to stabilize the output pulse current.

[0012] For purposes of sampling, the control loop measurements of pulse current level are taken at a rate considerably less than the frequency at which the output pulses are generated. The adjustment circuit of the control loop also performs at a relatively slow rate which further helps to conserve energy in the nerve stimulation system.

[0013] Preferably, the control loop includes a limit circuit for establishing predetermined high and low control limits for the current magnitude of the output pulses, and produces an adjustment of an appropriate parameter of the output pulses to return the output pulse current to a level within those limits whenever one of the limits is exceeded. Alternatively, the measurement circuit means may include means for performing successive approximations of the output current magnitude by measuring one output pulse per burst and completing the approximation after a sequence of the bursts.

[0014] In the preferred embodiment of the current stabilization mode system, the measurements are taken by sampling at the trailing edge of the selected output pulses. Alternatively, the sampling may be performed at the midpoint of the selected output pulses.

[0015] The charge stabilization mode functions in a similar way, but measures the charge delivered in each sample by integrating the sampled current over a preset time interval, specifically the output pulse duration, and compares that value to a target charge level. Any discrepancy between the two is reduced by adjusting the duration of the output pulses to maintain the charge delivered in the output pulses at a desired level for nerve cell membrane excitation.

[0016] Accordingly, it is a broad object of the present invention to provide an implantable excitable tissue stimulating device having reduced energy overhead.

[0017] A more specific object of the invention is to provide an improved implantable neurostimulator having an output circuit adapted to generate pulses in either a current stabilized mode or a charge stabilized mode for operating efficiency and conservation of battery power.

[0018] Another object of the invention is to provide apparatus and methods for stabilizing the output energy delivered from an implanted electrical device to excitable tissue of a patient to produce desired stimulation of the tissue without significant energy losses, by relatively frequent but not continuous measurement and adjustment of the output energy to a target level.

[0019] It is a further object of the present invention to achieve these and other objects of the invention by means of a stabilization system which performs sampling of the selected parameter of the output pulses of the tissue stimulator, such as a neurostimulator, rather than operating in a continuous measurement and adjustment mode.

Brief Description of the Drawings

[0020] The above and still further objects, features and attendant advantages of the invention will become apparent from a consideration of the following detailed description of the preferred embodiments thereof, taken in conjunction with the accompanying drawings, in which:

FIG. 1 is a simplified block diagram of an exemplary implantable neurostimulator in which the present invention may be utilized;

FIGS. 2A and 2B are, respectively, a phantom view illustrating the relative positions of the neurostimulator, nerve electrode array (implanted, for example, on the vagus nerve) and associated electrical leads implanted in the patient, and indicating associated external equipment; and a detailed view of the electrode array of FIG. 2A implanted on the selected nerve;

FIG. 3 is a simplified timing diagram of a typical output signal waveform of the neurostimulator of FIG. 1;

FIG. 4 is a block diagram of the circuitry employed in the neurostimulator of FIG. 1, to implement the preferred embodiment of the current stabilization mode of the invention; and

FIGS. 5A and 5B are block diagrams of alternative implementations of the charge stabilization mode of the invention, in the neurostimulator of FIG. 1.

Detailed Description of the Preferred Embodiments and Methods

[0021] According to the present invention, the output circuit of an excitable tissue stimulating implantable pulse generator may employ either of two output stabilization modes, namely (i) current stabilization or (ii) charge stabilization.

[0022] The current stabilization mode employs a constant voltage output circuit combined with a circuit including a digital control system, preferably comprising a microprocessor, which, among other things, measures the current in the output pulse waveform. The measurement may be made during each pulse or only during selected pulses of the output pulse sequence. The digital control system uses the measurement information to adjust the output voltage to stabilize the output current at a desired level or within predefined limits. Unlike prior art "constant current" devices, the control loop of the current stabilization mode consumes relatively little energy, i.e., has low "energy overhead", in part because the measurements need not be made in

every pulse cycle, and may be performed at a very slow rate over multiple output pulses. Adjustment of the energy in the output pulse waveform based on these measurements may also be performed at a relatively slow rate, which relieves the need for additional supply voltage to allow for compensation during the output pulses.

[0023] Preferably, the output current is alternately compared against predetermined high and low control limits, and the output voltage is varied only if an exception condition is determined to exist, that is, a condition in which the output current falls outside these set limits. If desired, the adjustment may be made for multiple cycles of an exception condition. Alternatively, the measurements may be performed over a sequence of pulses by successive approximations of the output, and adjustments made accordingly.

[0024] Output current level varies during a "constant voltage" output pulse, and therefore a definition of the output current magnitude to be maintained must be established. For example, the output current magnitude may be defined as that at the leading edge, or the midpoint, or the trailing edge of the pulse; or as the mean current during the pulse. The trailing edge current magnitude is the preferred designation for control purposes, to reduce system complexity. A trailing edge measurement can be performed with a relatively slow sampling circuit (in contrast, for example, to the requirement for a leading edge measurement), and does not require the generation of special timing control signals which must vary with programmed pulse duration.

[0025] An alternative to the preferred technique of measuring the current magnitude at the trailing edge, on a pulse sampling basis, is to perform the measurement at the midpoint of the output pulse. This is a close approximation of the mean current level of the sampled pulse, with a requirement of only minimal additional energy overhead. The sampling in this case could be biased toward the second half of the pulse, to improve the approximation.

[0026] FIG. 1 is a simplified block diagram of an exemplary stimulus (pulse) generator of an excitable tissue stimulating device to which the principles of the present invention may be applied. Such a device, a neurostimulator for example, although the present invention is not limited to that application, may be implanted in or employed external to a patient's body to treat and/or control various disorders by application of modulating electrical signals to selected tissue such as a nerve of the patient. The location of an implanted device for stimulating the patient's vagus nerve, and details of the lead and electrode system of the device are illustrated in Figs. 2A and 2B.

[0027] The neurostimulator utilizes a conventional microprocessor among other standard electrical and electronic components, and in the case of an implanted device, communicates by asynchronous serial communication with a programmer and/or monitor located external to the patient's body for controlling or indicating states of the device. Passwords, handshakes and parity checks are employed for data integrity. Pulse generator 10 of the neurostimulator may be adapted for implantation in the patient in a pocket formed by the surgeon just below the skin in the chest as shown in FIG. 2A, or may be a primarily external system. The neurostimulator also includes an implantable stimulating electrode array 40 and electrical lead system 42 (FIGS. 2A and 2B) for applying the output signal of generator 10 to the selected nerve, such as the vagus nerve. Components external to the patient's body include a computer 53 and wand 55 for telemetry of parameter programming to and monitoring signals from generator 10 (or an associated sensing circuit). The programmed stimulating output pulse sequence of the pulse generator is delivered to the nerve(s) to modulate the electrical activity thereof.

[0028] In the device of FIG. 1, generator 10 includes a battery (for example, a single lithium thionyl chloride cell) 12 and voltage regulator 15 to supply a clean, steady output voltage to other components of the device, including a logic and control section 17. The latter includes a microprocessor to control programmable functions of the device including current, frequency, pulse width, on-time and off-time of the output signal. The output signal may thus be tailored to achieve the desired modulation of electrical activity of the nerve. Timing signals for the logic and control functions of the generator are provided by a crystal oscillator 20. A magnetically-actuated reed switch 27 is incorporated in the electronics package to provide the capability for manual activation of the generator (e.g., by the patient, using an external magnet, not shown, placed immediately adjacent to the generator implant site). Built-in antenna 25 enables communication between the implanted pulse generator and the external electronics via the wand 55. Once the system is programmed, it maintains and operates at the programmed settings until reprogrammed (by the attending physician).

[0029] Logic and control section 17 controls an output circuit 22 which generates the output signal having parameters programmed to enable treatment of the disorder of interest. The output circuit and its programmed output signal are coupled to an electrical connector 30 on the housing 35 of generator 10 and, via the connector, to lead assembly 42 connected to the stimulating electrode array 40 (FIGS. 2A and 2B). Housing 35 is hermetically sealed and composed of a material such as titanium which is biologically compatible with the fluids and tissue of the patient's body. Further details of the structure and operation of the basic neurostimulator are set forth in the '895 application.

[0030] As shown in FIGS. 2A and 2B, nerve stimulating electrode array 40 is conductively connected to the distal end of insulated electrically conductive lead assembly 42 which is attached at its proximal end to connector 30 on the generator. Electrode array 40 may be a bipolar stimulating electrode of the type described

in U.S. Patent 4,573,481 to Bullara. In this example, the electrode array is surgically implanted on the vagus nerve 45 in the patient's neck. The two electrodes 43 and 44 are wrapped about the nerve, and the assembly is secured to the nerve by a spiral anchoring tether 47 of the type disclosed in U.S. Patent 4,979,511 to Reese S. Terry, Jr., assigned to the same assignee as the instant application. Lead assembly 42 is secured in place by a suture connection 50 to nearby tissue, but can flex with movement of the patient's chest and neck.

[0031] FIG. 3 is an idealized representation of an exemplary signal waveform which may be delivered by output circuit 22 of the neurostimulator pulse generator to electrode array 40, and is presented principally to clarify terminology, including signal-on time, signal-off time, signal frequency, pulse width, and output current.

[0032] A block diagram of a preferred embodiment of a control loop modification of output circuit 22 to implement the current stabilization mode of the invention is shown in FIG. 4. The control loop uses a digital control system which includes the microprocessor in logic/control section 17 to detect and measure the output signal of output circuit 22, and to supply a feedback signal for adjusting the current magnitude of the output pulses of the generator. Logic/control section 17 has several control and command function outputs from the microprocessor which are delivered variously to the output circuit and to the control loop 60. The output circuit includes a pair of switches (e.g., field effect transistors) 65, 67 which are actuated by command voltages from the microprocessor on paths 73 and 77, respectively. A signal voltage line 68 delivers the output pulses to the patient (via lead assembly 42 and electrode array 40), with the circuit completed through a return path 70 having a DC blocking capacitor 72 connected to the lead/electrode array.

[0033] When a pulse (or pulse sequence) is to be delivered to the nerve (i.e., signal-on time), switch 65 is turned on to deliver charge from storage capacitor 66 (according to the programmed pulse width and cycle/frequency) by commands on line 73 from the microprocessor. When switch 65 is on (and assuming a negative voltage on line 68 from the battery 12 or voltage regulator 15, and therefore on the storage capacitor 66), the output current flows from the capacitor through the ground path, through a low-valued (e.g., ten ohm) current sampling resistor 75, output path 70, blocking capacitor 72, the leads and nerve electrode, and back on path 68 to storage capacitor 66. When switch 65 is turned off, the voltage drops sharply to zero (from its higher negative value) with cessation of the pulse. The capacitor then recharges with the small amount of energy which was discharged, to the set output voltage level, in preparation for delivery of the next pulse.

[0034] With each pulse delivered to the nerve, there is an incremental build-up of charge on blocking capacitor 72 which, if left stored, could soon reach a level completely opposing the voltage delivered from the regulator and thereby rendering the output circuit ineffective. To prevent such an occurrence, the blocking capacitor is periodically discharged by turning switch 67 on with a command voltage from the microprocessor on line 77.

[0035] For purposes of stabilizing the output current, control loop circuit 60 periodically takes sample measurements of the output pulses, preferably at the trailing edge (or, alternatively, at the midpoint) of the pulse. The sampling is performed by a sample and hold circuit 80 which takes a reading of the current magnitude on line 81 from resistor 75, when actuated by a "sample current" command on line 84 from the microprocessor. To provide greater accuracy, the read value is boosted by the gain of an amplifier 85, which is calibrated based on a target (i.e., predetermined desired) current level from digital-to-analog (D/A) converter 86 supplied by a programmed digital value from the microprocessor on line 87.

[0036] The sample level is compared to the target level by comparator 88, which produces an output indicative of whether the sample level is greater or less than the target level, and the output information is fed back on line 90 to logic/control section 17. The output voltage level of the generated pulses is varied by an adjustment circuit 91 to reduce any discrepancy from the target current level. Adjustment circuit 91 is coupled to a programmable multiplier 92 in output circuit 22 (or other source of the final voltage level for the output pulses), which is nominally set by the microprocessor to multiply the battery voltage by any of a plurality of values (for example, 0.5, 1.0, 1.5, 2.0, 3.0) suitable to bring the output current level to the target level by corresponding adjustment of the output voltage of the pulses.

[0037] Adjustment circuit 91 includes a D/A converter 93 which receives a digital target voltage level on line 94 from the microprocessor 58, based on the results of the latest measurement performed by control loop circuit 60. This is compared, after conversion to an analog value, with the voltage level of the output from the programmable multiplier on line 68, in comparator 95. The output of the comparator on line 97 turns the multiplier on or off to produce the necessary adjustment according to the incremented setting of the multiplier by the microprocessor, to achieve the desired output current stabilization.

[0038] A charge stabilization mode of operation can achieve even greater energy savings than the current stabilization mode. Suitable embodiments and methods for implementing a charge stabilization mode for the output circuit of a tissue stimulating pulse generator according to the present invention will be described, by exemplary reference to nerve stimulation. It is known that the charge required to excite a cell membrane of excitable nerve tissue is relatively constant, within limits. At wide pulse widths, the charge required to be delivered increases as a result of decreased potential across the cell membrane. The decreased potential is attribut-

able to accommodation processes related to cell membrane active transport of ions. Within a range of pulse durations in the temporal vicinity of the membrane time constant, the energy required for stimulation is minimized.

[0039] Compensation for the membrane time constant must be considered. For any excitable cell which has fully recovered from previous stimulations, the voltage across its membrane which will cause regenerative depolarization is relatively constant over a wide range of pulse durations. For extremely short pulse widths (less than a few microseconds or tens of microseconds), however, this principle does not hold. Two competing factors determine the energy efficiency of stimulating pulses. For short duration pulses, resistive losses in the conducting medium reduce efficiency because the membrane behaves much as a capacitance. For a given voltage change across the membrane a fixed charge must be applied, and in the case of narrow pulses this is performed more rapidly by an inversely proportional increase in the delivered current. Although the current required to stimulate increases in inverse proportion to the output pulse duration, the energy loss in the surrounding medium varies as the square of the delivered current since energy is the time integral of the power. The power dissipated is equal to the resistance times the square of the current, assuming that the surrounding media are modeled as resistances, which is true of all but the pulse generator output capacitance and any electrode polarization.

[0040] If this were the only factor to be considered, then the wider the pulse the lower the energy required to stimulate, and a constant charge would be required at any pulse duration. When longer stimulating pulse durations are considered, the membrane model must be modified to include a parallel conductance to account for leakage through the membrane, active transport mechanisms in the membrane, and leakages around the membrane. As each output pulse charges the membrane, some charge bleeds away. This is well modeled by an integrator with bleeder resistance, which may be used in the control loop to more efficiently control the output pulses to induce the threshold charge across the excitable tissue membranes.

[0041] In the charge stabilization mode of the present invention, the charge delivered in an output pulse is monitored by integrating the current in the output pulse as a measure of the charge. That information is then used to adjust the output pulse duration of the neurostimulator generator within a predetermined range of pulse widths. Whenever the pulse width is outside this range, a multiplier setting may be changed appropriately to maintain the desired output charge.

[0042] Capacitive multipliers and dividers may be utilized to produce different relatively low voltages with greater efficiency than by use of other methods. Voltage levels related to the system input voltage (i.e., a battery voltage for implantable devices) can be produced with maximum efficiency as a simple ratio of integers. Ratios such as 1/3, 1/2, 2/3, 3/2, 2/1, 3/1, and 4/1 are easily obtained. In practical devices, these settings are probably too coarse for constant current control, but use of charge stabilization control with pulse duration as the primary control variable allows these relatively widely spaced voltages to achieve the desired results.

[0043] An algorithm may be used to maintain constant output charge in the presence of changing impedances or changing battery voltage. In theory, if the supply voltage is adequate, output charge stabilization may be provided over a broad range of pulse durations. For maximum energy efficiency, however, only pulse durations which are in the temporal neighborhood of the membrane time constant of target cells are optimum. If the time constant of the output circuit is shorter than or sufficiently close to the membrane time constant, the range of optimal pulse widths is modified to be of shorter duration. In either event, the device design and target cells serve to determine an appropriate range of pulse widths. If the output control algorithm produces pulse durations at or beyond these limits, the output voltage should be changed in a direction to return the pulse duration toward the optimum.

[0044] A preferred method resolves either situation, i.e., in which the pulse duration is too long or too short. In the former case, the voltage multiplier setting is increased by one step and the output voltage is slowly ramped up. During this ramp up time, the control loop functions to ramp down the output pulse duration. Ramping is ceased when the output voltage reaches a point that is efficiently produced by the new multiplier setting. In the case where the output pulse duration is too short, the output voltage is slowly ramped down, which causes a gradual increase in the output pulse duration. When the output voltage reaches a level that is efficiently producible at the next lower voltage multiplier setting, that setting is used and the ramping is ceased.

[0045] Use of such a charge stabilization control algorithm avoids problems which may be encountered by other algorithms which cause the voltage to be changed because the computed pulse duration is not within the allowed range. For example, an algorithm that changes two variables simultaneously by relatively large amounts may result in significant changes in effectiveness of tissue stimulation. The preferred method for the charge stabilization mode allows the voltage to be increased or decreased in relatively small regulated steps (which themselves may be produced relatively inefficiently) toward the next efficiently produced capacitor multiplier ratio. These intermediate steps are not stable, and the algorithm continues to step the voltage in the direction of the stable points.

[0046] The pulse duration region at or near which it is no longer true that the charge required to stimulate a nerve cell membrane is relatively constant for durations significantly less than the membrane time constant, coincides with pulse durations for which stimulation is

achieved with minimal energy. For a given membrane type these perturbations can be modeled from the ideal, and the model can then be used to make adjustments to the delivered pulse duration. One technique for accomplishing this is to modify the integrator which measures the delivered charge from the output current and time. As observed above, a bleeder resistance or current source may be added to the integrator to model the excitable cell's membrane ion pump activity. Maintaining the output of this system constant at the end of each output pulse, rather than simply maintaining the output charge constant on the same basis, serves to more accurately stabilize the tissue stimulation. The same goal may be achieved with a digital system. The curve relating threshold charge to pulse width is programmed into the control system, the measured charge is multiplied by the reciprocal of this curve, and the result is used as the regulated variable.

[0047] A pair of embodiments of a circuit for implementing the charge stabilization mode in conjunction with the output circuit 22 of neurostimulator generator 10 are shown in block diagrammatic form in FIGS. 5A and 5B. In both embodiments, the circuitry employed is substantially the same as that utilized for the current stabilization mode embodiment of FIG. 4, except for the control loop portion 60, with adjustment of output pulse duration. Accordingly, the description of the two charge stabilization mode embodiments will be substantially limited to a description of the modified control loop portion.

[0048] In the first implementation of the charge stabilization mode circuit, partially shown in FIG. 5A, the current taken from the sampling resistance 75 is applied to an integrator 102 controlled by the microprocessor in logic/control section 17 to perform an integration of pulse current over the output pulse duration time interval and to hold the results of the integration, in response to appropriate command inputs on line 104. The output of the integrator therefore represents the charge delivered in the respective output pulse sample. At the end of each sample interval, the integrator 102 is reset by a command from the microprocessor on line 105, in readiness for integration of the next sample.

[0049] The output level of the integrator is boosted in an amplifier 107 and applied to one input of a comparator 108. The other input to the comparator is from a D/A converter 110 which provides an analog value of a target charge level from the digital value thereof inputted from the microprocessor. Any discrepancy between the two values under comparison is reflected at the output 112 of the comparator, and is utilized to adjust the duration of the output pulses to stabilize the charge delivered in the output pulses. If too little charge has been delivered, the pulse durations are increased; if too much charge is delivered, the pulse durations are decreased.

[0050] In the alternative implementation of the charge stabilization mode portion shown in FIG. 5B, a similar operation is performed to that of FIG. 5A except that provision is made for membrane loss modelling as generally described above. The integrator which derives a measure of the charge delivered in a sampled pulse by integrating the pulse current over a preset time is modified by using a resistance or current source 120 to model the cell membrane repolarization for excitation. In essence, the bleeder resistance or current source 120 across amplifier 121 models the situation in which the charge is being bled off as the output pulse is seeking to charge the cell membrane. The amplifier circuit acts like an integrator in summing its inputs over time. Commands 123 and 125 from the microprocessor activate switches 124 and 126 respectively. A comparator 128 receives inputs from the modelled cell membrane repolarization and from a D/A converter 130 provides the target charge level from the microprocessor. Here again, the discrepancy from the comparison at output 132 is used to adjust the duration of the output pulses to stabilize the charge delivered in the output pulses. The control loop circuit operates to maintain the membrane charge constant (at a programmed value) at the end of each output pulse, which has the effect of stabilizing the tissue stimulation.

[0051] It will be seen from the foregoing description that output stabilization systems constructed according to the principles of the present invention provide superior energy conservation in either the current stabilization mode or the charge stabilization mode, without sacrificing system performance and, indeed, while improving operating efficiency.

Claims

1. A body implantable, battery operated nerve tissue stimulator for delivering stimulating pulses to selected nerve tissue of a patient, especially a stimulator of the vagus nerve of a patient, the stimulator being operable via one or more electrodes (40) implantable on or near the tissue (45), the stimulator having a pulse generator (10) for sequentially generating output pulses in a programmable pattern for application to the selected nerve tissue, the pulse generator including a programmable output system (22) for selectively varying the electrical parameters of the output pulses to provide the desired tissue stimulation, **characterized in that** a control loop (60) of the output system performs periodic measurements of the magnitude of a preselected parameter of the output pulses on a sampling basis at a predetermined point in the excursion of the output pulses selected for sampling, where the sampling rate is considerably below the rate at which the output pulses are generated, compares each sampled magnitude of the preselected parameter to a target value for the parameter, and responds to differences between the sampled magnitude and the target value for the

parameter to null the difference by relatively slow adjustment compared to the output pulse rate and thereby stabilize the magnitude of the preselected parameter to provide a source of pulses in which the preselected parameter is substantially constant throughout for application to the selected nerve tissue without changing the rate at which the output pulses are generated.

2. The nerve tissue stimulator of claim 1, in which the periodic measurements of magnitude of the preselected parameter are performed over separated cycles of the output pulses.

3. The nerve tissue stimulator of either of the preceding claims, in which the predetermined parameter is electrical current delivered in each output pulse, the magnitude of the current is measured in at least one but less than all of the output pulses in a burst of output pulses, and successive approximation of the magnitude of the current of the selected output pulses is performed by the control loop (60) and the approximation is completed after a sequence of bursts.

4. The nerve tissue stimulator of claim 1 or 2, in which the predetermined parameter is electrical current delivered in each output pulse, the magnitude of the current is measured in at least one but less than all of the output pulses in a burst of output pulses, and predetermined high and low control limits are established for the current magnitude of the output pulses and the current magnitude of selected ones of the output pulses is alternately compared against the established high and low control limits by the control loop, and further including means in the control loop for varying the voltage of the output pulses to bring the magnitude of the current of the output pulses within the established limits when the comparison indicates that either limit is exceeded.

5. The nerve tissue stimulator of claim 4, in which the magniitude of the current of the output pulses is brought within the established limits only when the comparison indicates that either limit is exceeded by multiple output pulses of each sequence.

6. The nerve tissue stimulator of any of the preceding claims, in which the predetermined point in the excursion of the output pulses selected for sampling is the trailing edge of the respective selected pulses.

7. The nerve tissue stimulator of any of claims 1 to 5, in which the predetermined point in the excursion of the output pulses selected for sampling is the approximate midpoint of the respective selected pulses.

8. The nerve tissue stimulator of either of claims 1 or 2, in which the preselected parameter is electrical charge delivered in each output pulse, and the control loop adjusts the duration of each of the output pulses to null the difference between the sampled magnitude and the target value for the electrical charge in the selected output pulses.

9. The nerve tissue stimulator of claim 8, in which predetermined high and low control limits are established for the magnitude of the electrical charge in the output pulses and the magnitude of the electrical charge in selected ones of the output pulses is alternately compared against the established high and low control limits by the control loop, and further including means in the control loop for varying the duration of the output pulses to bring the magnitude of the electrical charge of the output pulses within the established limits when the comparison indicates that either limit is exceeded.

10. The nerve tissue stimulator of either of claim 8 or 9, in which the control loop includes means for integrating the electrical current in the output pulses over a predetermined time interval to determine the magnitude of the electrical charge delivered at each output pulse.

11. The nerve tissue stimulator of any of claims 8 to 10, in which the control loop includes means for modeling the excitable cell membrane repolarization of the selected nerve tissue to control the duration, of the output pulses to induce a threshold electrical charge across the membrane sufficient for excitation of the membrane.

12. The nerve tissue stimulator of any of claims 8 to 10, in which the control loop includes means for modeling the charge delivered in each output pulse to induce a threshold charge across the excitable cell membranes of the nerve tissue selected to be stimulated which accounts for charge loss attributable to leakage from the membranes.

13. The nerve tissue stimulator of either of claim 8 or 9, in which the control loop includes means for immediately ending each output pulse when the target value is reached.

Patentansprüche

1. In den Körper implantierbarer batteriebetriebener Nervengewebestimulator zum Liefern von Stimulationsimpulsen an ausgewähltes Nervengewebe eines Patienten, insbesondere Stimulator für den Vagusnerven eines Patienten, wobei der Stimulator über eine oder mehrere an oder nahe dem Gewebe (45) implantierbare Elektroden (40) betrieben wird,

wobei der Stimulator einen Impulsgenerator (10) aufweist, um sequentiell Ausgangsimpulse in einem programmierbaren Muster für die Anwendung auf das ausgewählte Nervengewebe zu erzeugen, wobei der Impulsgenerator ein programmierbares Ausgangssystem (22) aufweist, um selektiv die elektrischen Parameter der Ausgangsimpulse zu variieren, um die gewünschte Nervenstimulation zu liefern, dadurch gekennzeichnet, dass eine Steuerschaltung (60) des Ausgangssystemes

- periodische Messungen der Größe eines ausgewählten Parameters der Ausgangsimpulse auf einer Abtastbasis zu einem vorbestimmten Zeitpunkt bei der Ausführung der für das Abtasten ausgewählten Ausgangsimpulse vornimmt, wobei die Abtastrate erheblich unter der Rate liegt, mit der die Ausgangsimpulse erzeugt werden,
- jede abgetastete Messgröße des ausgewählten Parameters mit einer Zielgröße für den Parameter vergleicht und auf die Differenzen zwischen der abgetasteten Messgröße und dem Zielwert für den Parameter antwortet, um die Differenz durch verglichen mit der Rate der Ausgangsimpulse relativ langsame Einstellung zu Null zu machen und dadurch die Messgröße des vorbestimmten Parameters zu stabilisieren, um eine Pulsquelle bereitzustellen, mit der der ausgewählte Parameter während der Anwendung auf das ausgewählte Nervengewebe im wesentlichen konstant ist, ohne die Rate zu ändern, mit der die Ausgangsimpulse erzeugt werden.

2. Nervengewebestimulator nach Anspruch 1, bei dem die periodischen Messungen der Messgröße des ausgewählten Parameters über unterschiedliche Zyklen von Ausgangsimpulsen durchgeführt werden.

3. Nervengewebestimulator nach einem der vorhergehenden Ansprüche, bei dem der vorbestimmte Parameter der bei jedem Ausgangsimpuls gelieferte elektrische Strom ist, wobei die Größe des Stromes bei zumindest einem, aber weniger als allen Ausgangsimpulsen in einem Bündel von Ausgangsimpulsen gemessen wird und wobei durch die Steuerschaltung (60) eine sukzessive Annäherung der Größe des Stromes der ausgewählten Ausgangsimpulse durchgeführt und die Annäherung nach einer Folge von Bündeln abgeschlossen ist.

4. Nervengewebestimulator nach Anspruch 1 oder 2, bei dem der vorbestimmte Parameter der bei jedem Ausgangsimpuls gelieferte elektrische Strom ist, wobei die Größe des Stromes in zumindest einem, aber weniger als allen Ausgangsimpulsen in einem Bündel von Ausgangsimpulsen gemessen wird und wobei vorbestimmte hohe und niedrige Steuergrenzwerte für die Größe des Stromes der Ausgangsimpulse aufgestellt werden und die Größe des Stromes von ausgewählten einzelnen Ausgangsimpulsen alternativ mit dem hohen bzw. niedrigen Steuergrenzwert durch die Steuerschaltung verglichen werden, wobei ferner in der Steuerschaltung eine Einrichtung vorgesehen ist, um die Spannung der Ausgangsimpulse zu variieren, um die Größe des Stromes der Ausgangsimpulse in dem Bereich zwischen den aufgestellten Grenzwerten zu bringen, wenn der Vergleich anzeigt, dass eine der Grenzwerte überschritten wird.

5. Nervengewebestimulator nach Anspruch 4, bei dem die Größe des Stromes der Ausgangsimpulse in den Bereich zwischen den aufgestellten Grenzwerten nur dann gebracht wird, wenn der Vergleich anzeigt, dass einer der Grenzwerte durch mehrere Ausgangsimpulse in jeder Sequenz überschritten wird.

6. Nervengewebestimulator nach einem der vorhergehenden Ansprüche, bei dem der vorbestimmte Zeitpunkt im Verlauf der für das Abtasten ausgewählten Ausgangssignale die rückwärtige Flanke der jeweiligen ausgewählten Impulse ist.

7. Nervengewebestimulator nach einem der Ansprüche 1 bis 5, bei dem der vorbestimmte Zeitpunkt im Verlauf der für das Abtasten ausgewählten Ausgangssignale ungefähr der Mittelpunkt der jeweiligen ausgewählten Impulse ist.

8. Nervengewebestimulator nach Anspruch 1 oder 2, bei dem der ausgewählte Parameter die mit jedem Ausgangsimpuls gelieferte elektrische Ladung ist und die Steuerschaltung die Dauer jedes Ausgangsimpulses einstellt, um die Differenz zwischen der abgetasteten Messgröße und dem Zielwert für die elektrische Ladung in den ausgewählten Ausgangsimpulsen zu Null zu machen.

9. Nervengewebestimulator nach Anspruch 8, bei dem der vorbestimmte hohe und niedrige Steuergrenzwert für die Messgröße der elektrischen Ladung in den Ausgangssignalen aufgestellt werden und die Größe der elektrischen Ladung in ausgewählten Ausgangsimpulsen durch die Steuerschaltung mit dem aufgestellten hohen und niedrigen Steuergrenzwert alternativ verglichen werden, wobei ferner eine Einrichtung in der Steuerschaltung vorgesehen ist, um die Dauer der Ausgangsimpulse zu variieren, um die Größe der elektrischen Ladung der Ausgangsimpulse in den

Bereich zwischen den aufgestellten Grenzwerten zu bringen, wenn der Vergleich anzeigt, dass einer der Grenzwerte überschritten wird.

10. Nervengewebestimulator nach Anspruch 8 oder 9, bei dem die Steuerschaltung eine Einrichtung zum Integrieren des elektrischen Stromes in den Ausgangsimpulsen über ein vorbestimmtes Zeitintervall aufweist, um die Größe der mit jedem Ausgangsimpuls gelieferten elektrischen Ladung zu bestimmen.

11. Nervengewebestimulator nach einem der Ansprüche 8 bis 10, bei dem die Steuerschaltung eine Einrichtung zum Formen der Repolarisation der erregbaren Zellmembranen des ausgewählten Nervengewebes zur Steuerung der Dauer der Ausgangsimpulse aufweist, um eine elektrische Schwellenladung über die Membran zu induzieren, die für eine Anregung der Membran ausreichend ist.

12. Nervengewebestimulator nach einem der Ansprüche 8 bis 10, bei dem die Steuerschaltung eine Einrichtung zum Formen der bei jedem Ausgangsimpuls gelieferten Ladung aufweist, um eine Schwellenladung über die erregbaren Zellmembranen des für eine Stimulation ausgewählten Nervengewebes zu induzieren, die den Ladungsverlust aufgrund des Schwundes an den Membranen berücksichtigt.

13. Nervengewebestimulator nach einem der Ansprüche 8 oder 9, bei dem die Steuerschaltung eine Einrichtung aufweist, um jeden Ausgangsimpuls unmittelbar zu beenden, wenn der Zielwert erreicht ist.

Revendications

1. Stimulateur de tissu nerveux actionné par une pile et implantable dans le corps pour fournir des impulsions de stimulation à un tissu nerveux choisi d'un patient, en particulier un stimulateur du nerf vague d'un patient, le stimulateur étant actionnable par une ou plusieurs électrodes (40) implantables sur le tissu (45) ou près de celui-ci, le stimulateur comportant un générateur d'impulsions (10) pour produire séquentiellement selon une configuration programmable des impulsions de sortie à appliquer au tissu nerveux choisi, le générateur d'impulsions comprenant un système de sortie programmable (22) pour faire varier sélectivement les paramètres électriques des impulsions de sortie pour stimuler le tissu désiré, caractérisé en ce qu'une boucle de commande (60) du système de sortie réalise des mesures périodiques de l'amplitude d'un paramètre prédéterminé des impulsions de sortie sur une base d'échantillonnage à un point prédéterminé dans l'excursion des impulsions de sortie sélectionnées pour l'échantillonnage, le taux d'échantillonnage étant très inférieur au taux auquel les impulsions de sortie sont produites, compare chaque amplitude échantillonnée du paramètre prédéterminé à une valeur cible pour le paramètre, et répond aux différences entre l'amplitude échantillonnée et la valeur cible pour le paramètre de façon à annuler la différence par réglage relativement lent par rapport à la cadence des impulsions de sortie, et pour stabiliser ainsi l'amplitude du paramètre prédéterminé pour fournir une source d'impulsions dans laquelle le paramètre prédéterminé est sensiblement constant pour être appliqué au tissu nerveux choisi sans changer la cadence à laquelle les impulsions de sortie sont produites.

2. Stimulateur de tissu nerveux selon la revendication 1, dans lequel les mesures périodiques d'amplitude du paramètre prédéterminé sont réalisées sur des cycles séparés des impulsions de sortie.

3. Stimulateur de tissu nerveux selon l'une quelconque des revendications précédentes, dans lequel le paramètre prédéterminé est un courant électrique délivré dans chaque impulsion de sortie, l'amplitude du courant est mesurée dans au moins une mais pas dans toutes les impulsions de sortie dans une salve d'impulsions de sortie, et des approximations successives de l'amplitude du courant des impulsions de sortie sélectionnées sont réalisées par la boucle de commande (60) et l'approximation est achevée après une séquence de salves.

4. Stimulateur de tissu nerveux selon la revendication 1 ou 2, dans lequel le paramètre prédéterminé est le courant électrique fourni dans chaque impulsion de sortie, l'amplitude du courant est mesurée dans au moins une mais pas dans toutes les impulsions de sortie dans une salve d'impulsions de sortie, et des limites de commande haute et basse prédéterminées sont établies pour l'amplitude du courant des impulsions de sortie et l'amplitude du courant des impulsions de sortie sélectionnées est alternativement comparée aux limites établies haute et basse par la boucle de commande, et comprenant en outre des moyens dans la boucle de commande pour faire varier la tension des impulsions de sortie pour amener l'amplitude du courant des impulsions de sortie à l'intérieur des limites établies quand la comparaison indique que l'une ou l'autre limite est dépassée.

5. Stimulateur de tissu nerveux selon la revendication 4, dans lequel l'amplitude du courant des impulsions de sortie est amenée à l'intérieur des limites établies seulement quand la comparaison indique

que l'une ou l'autre des limites est dépassée par des impulsions de sortie multiples de chaque séquence.

6. Stimulateur de tissu nerveux selon l'une quelconque des revendications précédentes, dans lequel le point prédéterminé dans l'excursion des impulsions de sortie sélectionnées pour l'échantillonnage est le front descendant des impulsions sélectionnées respectives.

7. Stimulateur de tissu nerveux selon l'une quelconque des revendications 1 à 5, dans lequel le paramètre prédéterminé dans l'excursion des impulsions de sortie sélectionnées pour l'échantillonnage est sensiblement le point milieu des impulsions sélectionnées respectives.

8. Stimulateur de tissu nerveux selon l'une des revendications 1 ou 2, dans lequel le paramètre prédéterminé est la charge électrique fournie dans chaque impulsion de sortie et la boucle de commande règle la durée de chacune des impulsions de sortie pour annuler la différence entre l'amplitude échantillonnée et la valeur cible pour la charge électrique dans les impulsions de sortie sélectionnées.

9. Stimulateur de tissu nerveux selon la revendication 8, dans lequel les limites de commande haute et basse sont établies pour l'amplitude de la charge électrique dans les impulsions de sortie et l'amplitude de la charge électrique dans les impulsions de sortie sélectionnées est alternativement comparée aux limites de commande haute et basse par la boucle de commande, et comprenant en outre des moyens dans la boucle de commande pour faire varier la durée des impulsions de sortie pour amener l'amplitude de la charge électrique des impulsions de sortie à l'intérieur des limites établies quand la comparaison indique que l'une ou l'autre des limites est dépassée.

10. Stimulateur de tissu nerveux selon l'une des revendications 8 ou 9, dans lequel la boucle de commande comprend des moyens pour intégrer le courant électrique dans les impulsions de sortie sur un intervalle de temps prédéterminé pour déterminer l'amplitude de la charge électrique fournie à chaque impulsion de sortie.

11. Stimulateur de tissu nerveux selon l'une quelconque des revendications 8 à 10, dans lequel la boucle de commande comprend des moyens pour modéliser la repolarisation de membranes de cellules excitables du tissu nerveux choisi pour commander la durée des impulsions de sortie pour induire une charge électrique de seuil sur la membrane suffisante pour exciter la membrane.

12. Stimulateur de tissu nerveux selon l'une quelconque des revendications 8 à 10, dans lequel la boucle de commande comprend des moyens pour modéliser la charge fournie lors de chaque impulsion de sortie pour induire une charge de seuil aux bornes des membranes des cellules excitables du tissu nerveux choisi pour être simulé, qui tiennent compte de la perte de charge attribuable à une fuite à partir des membranes.

13. Stimulateur de tissu nerveux selon l'une des revendications 8 ou 9, dans lequel la boucle de commande comprend des moyens pour arrêter immédiatement chaque impulsion de sortie quand la valeur cible est atteinte.

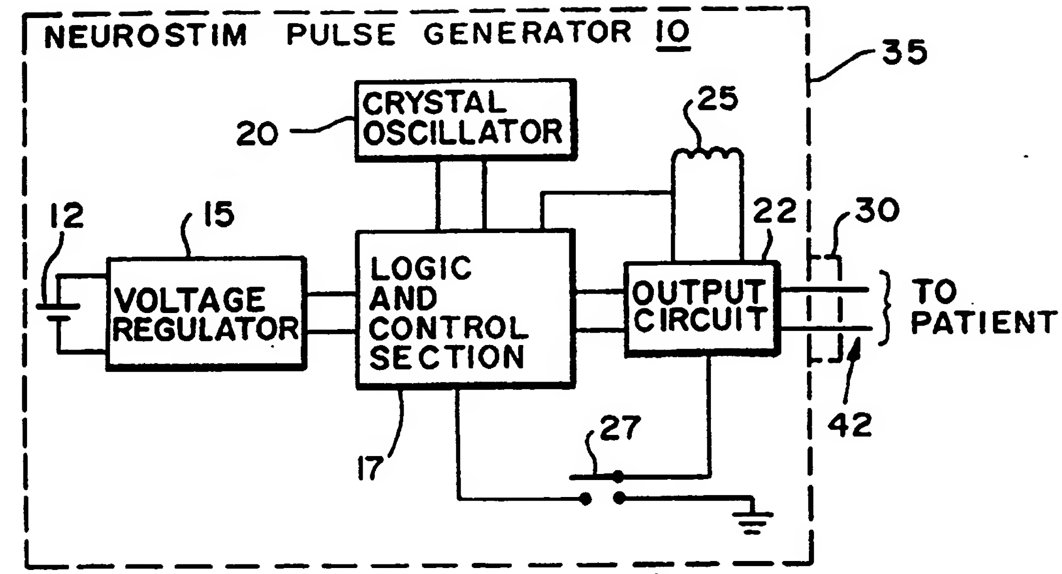
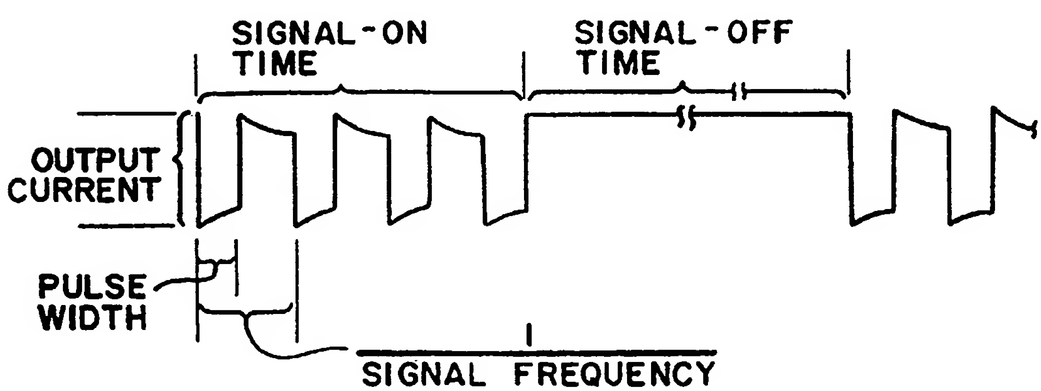
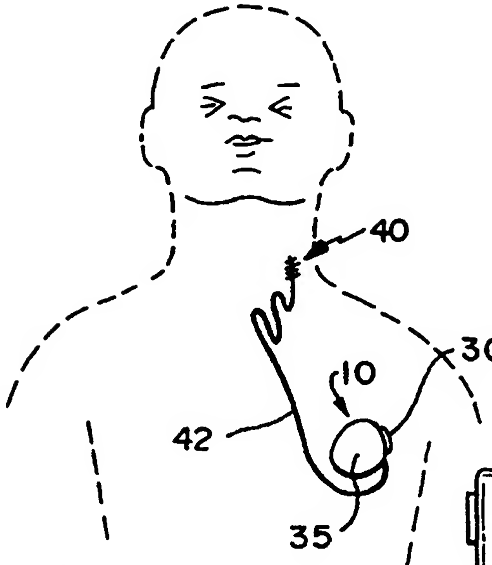

NEUROSTIM PULSE GENERATOR 10
35
CRYSTAL OSCILLATOR
20
25
12
15
22
30
VOLTAGE REGULATOR
LOGIC AND CONTROL SECTION
OUTPUT CIRCUIT
TO PATIENT
42
27
17

FIG. 1

FIG. 3


SIGNAL-ON TIME
SIGNAL-OFF TIME
OUTPUT CURRENT
PULSE WIDTH
SIGNAL FREQUENCY



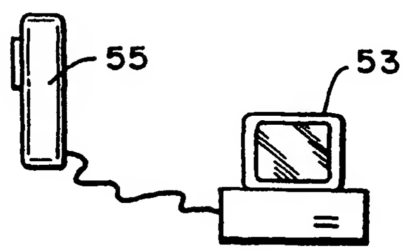


FIG. 2A

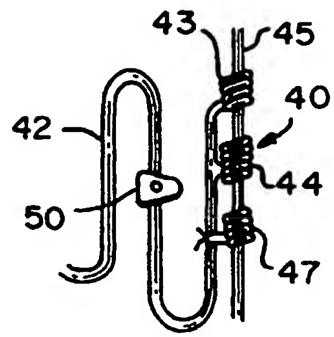
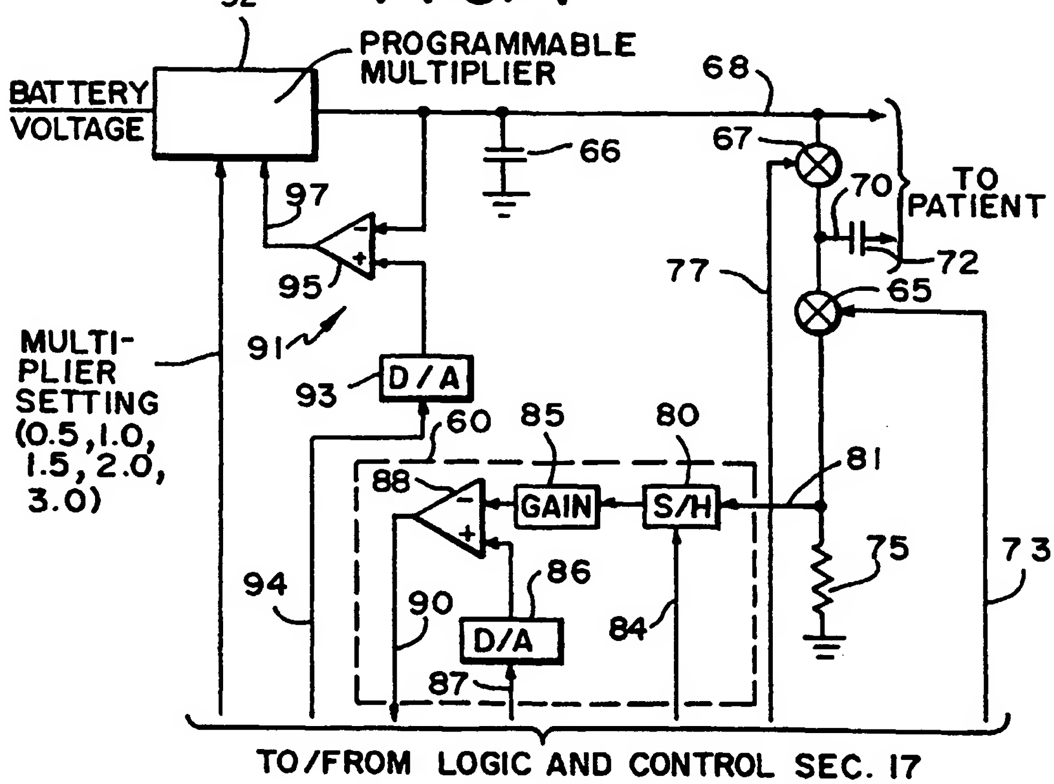


FIG. 2B

FIG. 4



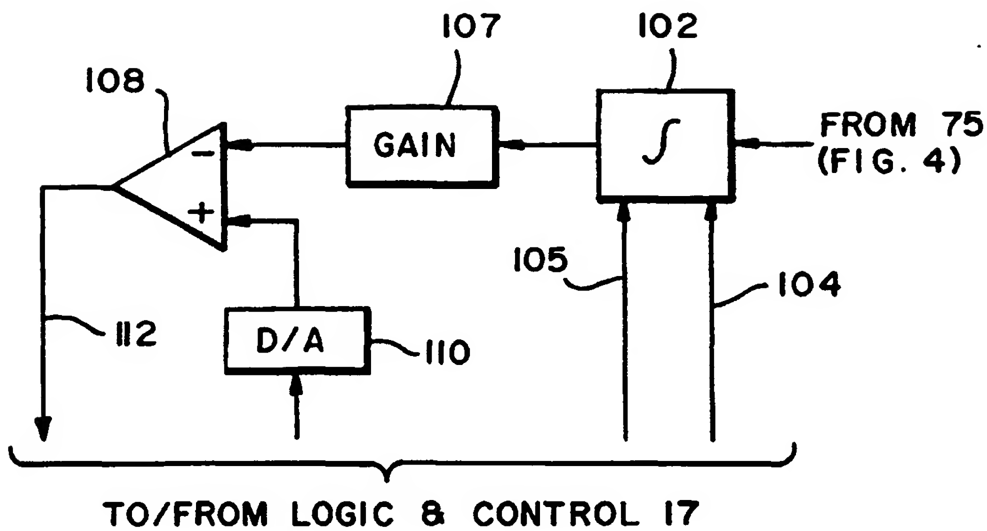

107
102
108
GAIN
FROM 75
(FIG. 4)
105
104
112
D/A
110
TO/FROM LOGIC & CONTROL 17

FIG. 5A

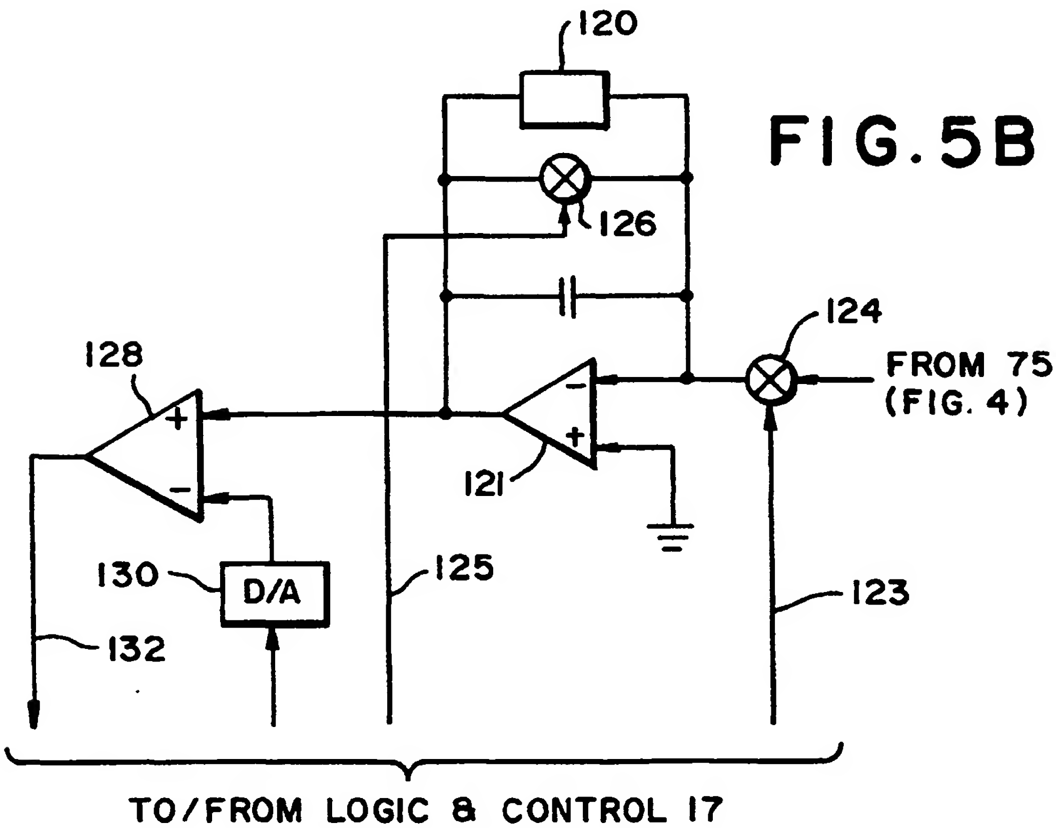

120
126
124
128
FROM 75
(FIG. 4)
121
130
D/A
125
123
132
TO/FROM LOGIC & CONTROL 17

FIG.5B